APPENDIX Y

Boehringer's Grounds for Appeal filed August 1, 2005

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Boards of Appeal

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Ka/Os

Re.: European Patent No. 0 830 142
European Patent Application No. 96.915746.0-2402
Boehringer Ingelheim Vetmedica, Inc.
T0603/05-334

Further to the Notice of Appeal filed with letter of May 20, 2005, we herewith submit the grounds of appeal.

1. Requests

As main request it is respectfully requested that the decision of the Opposition Division dated March 22, 2005 be set aside and the European Patent 830 142 be maintained in its granted form.

In the event that the Board of Appeal is not in a position to maintain EP 0 830 142 in its granted form on the basis of the written submissions, oral proceedings are requested in accordance with Article 116 EPC.

As first to fifth auxiliary request it is requested that the impugned decision be set aside and EP 0 830 142 be maintained on the basis of the enclosed claims entitled "Auxiliary Request 1", "Auxiliary Request 2", "Auxiliary Request 3", "Auxiliary Request 4" and "Auxiliary Request 5", respectively.

The proprietor reserves the right to submit amended claims depending on the course of the appeal proceedings. We refer to our submissions during the examination and opposition proceedings of the above patent. We further refer to the documents submitted during these proceedings, in particular the declaration by Professor Dr. Murtaugh filed with letter of September 22, 2004 and the experimental reports 623-850-92P-010, 623-850-92P-041 and 623-850-93P-004 annexed thereto.

2. Amended Claims

2.1 Claims 1, 4 and 13 of the first auxiliary request have been amended to specify that the attenuated virus does not shed. This feature is based on the disclosure at page 27, last paragraph of the original application text.

2.2 It has been specified in claims 1, 4 and 13 of the second auxiliary request that the vaccine is a safe vaccine. This feature is explicitly disclosed in Example 6, e.g. on page 23, lines 22/23 of the application text as originally filed.

2.3 It has been specified in claims 1, 4 and 13 of the third auxiliary request that treatment with the vaccine has no severe undesirable effects on the treated animals. Explicit basis for this feature can be found at page 16, lines 9-11 of the application as originally filed.

2.4 Claims 1, 4 and 13 of the fourth auxiliary request have been amended to clarify that treatment with the vaccine has no adverse effect on body (rectal) temperature of the treated animals. This feature is disclosed throughout the original application, see, e.g., page 12, lines 4-6 in combination with page 10, lines 32-34 and page 11, lines 3-6; or page 16, lines 9-11 in combination with page 15, lines 3-11.

2.5 The claims of the fifth auxiliary request correspond to the method claims as granted.

3. The subject matter of EP 830 142

"Porcine reproductive and respiratory syndrome" (PRRS) also referred to as "mystery swine disease" causes reproductive failure and produces respiratory distress in young pigs. Affected pigs may exhibit depression, lethargie, phyrexia and occasional vomiting. Further,

diseased piglets grow slowly, have respiratory distress and increased mortality. There are serious economic consequences of this devastating disease.

It is an object of EP 830 142 (hereinafter referred to as the contested patent) to provide an attenuated form of the virus which is suitable for use as master seed virus for the preparation of a safe vaccine.

The inventors of the contested patent surprisingly found that passaging the virus ATCC-VR2332 at least 70 times in the cell line MA-104 results in an attenuated virus which has all desirable properties that render it suitable for use as a master seed virus. These properties include that the attenuated virus when administered to swine, fails to cause clinical signs of PRRS disease (1), but is capable of inducing an immune response that immunizes the swine against pathogenic forms of PRRS virus (2). In addition, the attenuated virus is safe for use (3) and lacks shedding from the vaccinated pigs (4).

(1) Failure to cause clinical signs of PRRS disease upon vaccination has been shown in Examples 3 and 4 of the contested patent (see, in particular, paragraphs [0048] and [0066]).

(2) Examples 3 and 4 further show that vaccination with the attenuated virus according to the invention confers protection against the challenge with virulent PRRS virus (see, e.g. paragraphs [0058] and [0079]). The attenuated virus when administered to swine is thus capable of inducing an immune response that immunizes the swine against pathogenic forms of PRRS virus.

(3) Example 6 demonstrates that the vaccine as claimed in claim 1 is safe to use. The vaccine of the contested patent does not have any undesirable effects on the treated animals, such as fever, leukopenia or insufficient weight gain. Safety of the vaccine has been confirmed in the experimental report '004 submitted as part of the annex to Professor Dr. Murtaugh's declaration filed with letter of September 22, 2004 (cf. the sentence bridging pages 10/11). Also Examples 3 and 4 of the contested patent confirm the safety of the attenuated virus passaged at least 70 times.

(4) Lack of shedding of the attenuated virus according to this invention has been demonstrated in the experimental reports '041 and '004 submitted with letter of September

22, 2004. Viral shedding is the transmission of virus from infected animals to previously non-infected animals. Obviously, an attenuated virus which is to be used for the preparation of a vaccine should not shed from vaccinated pigs to non-vaccinated pigs.

4. The decision of the Opposition Division

The Opposition Division found that document D1 did not teach passaging at least 37 times, let alone passaging at least 70 times (page 6, 2nd full paragraph of the decision). The proprietor concurs with this view.

However, the Opposition Division found that the difference in number of passages indicated in claim 1 did not render the claimed subject matter novel. The Opposition Division was of the opinion that the number of passages which the virus underwent did not define the nature of the virus and that the virus resulting from passaging could not be predicted on the basis of the number of passages carried out in a specific cell line. Accordingly, the Opposition Division completely ignored the feature that the virus is passaged at least 70 times in cell culture of the monkey kidney cell line MA-104 and concluded that claim 1 as granted lacked novelty in view of document D1.

The proprietor respectfully disagrees with this finding of the Opposition Division and submits that the claims as granted are novel over the disclosure of document D1.

5. Novelty

5.1 The proprietor disagrees with the finding of the Opposition Division that the non-shedding nature of the virus was not an inherent feature of the virus claimed in claim 1. It is respectfully submitted that Professor Dr. Murtaugh, with the support of a passaging study, determined that the non-shedding of a virus as claimed in claim 1 was reproducible and repeatable. The opponent did not bring any evidence to counter the conclusions made by Dr. Murtaugh's declaration nor the evidence he relied upon to arrive at such a conclusion. Accordingly, it does not appear as though the Opposition Division gave sufficient weight to the considered opinion of a recognized expert in the field of PRRS virus.

With respect to the argument that further passaging may result in further mutations that are unpredictable which in turn might indicate that the loss of shedding resulting from passaging was also unpredictable, we respectfully disagree. While it is true that passaging of virus may result in the loss of some desired characteristics and the gain of some undesirable characteristics, this is not necessarily true for inherent characteristics, such as the attenuation and loss of shedding accomplished through passaging of VR-2332, as set forth in the claims.

When a particular loss or gain of a characteristic is shown to be repeatable and reproducible, it can be considered an inherent result of the passaging. This is true for the attenuation of VR-2332, which may be acquired prior to 70 passages, as well as the non-shedding characteristic, which is acquired after 70 passages of VR-2332 in the claimed cell line.

The proprietor has shown by comparative testing that the passage 70 virus does not shed. Professor Dr. Murtaugh has declared that this inherent property of shedding elimination is repeatable and reproducible. The proprietor has further shown by comparative testing that the passage 37 virus according to D1 continues to shed, and that passaging 50 times with cold adaptation does not provide the benefit of shedding elimination. Contrary thereto, the opponent did not bring any evidence to counter these experimental data. Therefore, the burden of proof to show that the elimination of shedding is not an inherent characteristic of the claimed vaccine now rests with the opponent.

Accordingly, all of the evidence of record substantiates our claim that the virus claimed in the patent differs from the virus of D1 and that this difference results from the passaging of the virus at least 70 times. The subject matter of claim 1 as granted is novel over the disclosure of document D1.

The proprietor reserves the right to submit further experimental data to prove that the non-shedding property is an inherent feature of a virus that has been passaged at least 70 times, as set forth in the claims, should this be contested by opponent. It has been specified in the claims of the first auxiliary request that the virus does not shed.

5.2 An attenuated virus to be used for the preparation of a vaccine composition is preferably safe for use, i.e. the vaccination itself should not have any adverse effects on the

vaccinated animals. A parameter that can be monitored with respect to safety is the body temperature post vaccination.

5.2.1 The specification of the contested patent demonstrates in several examples that the claimed vaccine composition comprises an attenuated virus which does not have an adverse effect on body temperature of the treated animals (see e.g. paragraph [0050] in combination with page 7, lines 35/36 and paragraph [0045]; paragraph [0069] in combination with [0062]/[0063]; and example 6). This is further confirmed by the Experimental Report '004 in the paragraph bridging pages 10 and 11:

> *"There was no safety problem as shown by the normal clinical observations of the pigs throughout the trial period and the absence of rise in the body temperature or decrease in white blood cell counts during the 14 day trial period"*

5.2.2 Document D1 is silent with respect to the safety of the cold-adapted virus passaged 37 times. This virus passaged 37 times has been tested for safety in the '010 Experimental Protocol. The animals of "group D" have been vaccinated with this virus. The animals of "group A" have been vaccinated with virulent passage 3 virus. As can be seen from page 2 of the "SUMMARY OF RESULTS", the animals of group D get fever upon vaccination. The fever begins on or before day 3 post vaccination and persists until at least day 14 post vaccination. The report summarizes the studies on body temperature as follows:

> *"Results of above show control pigs normal, while all vaccinated groups showed temperature >104°F with groups C and B having lower total positive score than* ***groups A and D which were most severe."***
> (page 2 of " SUMMARY OF RESULTS", emphasis added)

These results demonstrate that vaccination with a virus according to D1 passaged 37 times has an adverse effect on the body temperature of the treated animals.

In contrast thereto, the body temperature of vaccinated animals is not adversely affected by vaccination with the vaccine according to the contested patent.

Accordingly, the virus disclosed in D1 has properties that are unsuitable for a safe vaccine. Therefore, the virus of D1 cannot be novelty destroying for claim 1 as granted.

5.2.3. It has been specified in claim 1 of the second auxiliary request that a safe vaccine composition is claimed. The claims of the third and fourth auxiliary request specify that treatment with the vaccine according to the contested patent has no severe undesirable effects on the treated animals and no adverse effect on body temperature of the treated animals, respectively.

These claims are clearly novel over the disclosure of D1.

6. Inventive Step

D1 may be considered as closest prior art. The subject matter of claim 1 of the contested patent differs from the disclosure of D1 at least in that the virus is passaged at least 70 times. This difference causes the effect that the resulting vaccine has no severe undesirable effects on the vaccinated animals. Additionally, the claimed vaccine has an additional inherent advantage in that it does not shed.

The problem may therefore be formulated as the provision of a safe vaccine that has no severe undesirable effects on the vaccinated animals and does not shed.

The claimed solution to this problem would not have been obvious to the skilled person:

D1 neither teaches nor suggests that a safe vaccine could be obtained by passaging at least 70 times. Additionally, there is no hint that passaging at least 70 times would result in the elimination of shedding.

The risk of losing desirable characteristics or acquiring undesirable characteristics would have further motivated those of skill in the art to stop passaging the virus. Accordingly, those of skill in the art would not have been motivated to go beyond the 37 passages disclosed in D1, especially in view of the fact that it was not known if shedding could be eliminated by further passaging. Because continued passaging up to 50 total passages has been shown

by the patentee to not affect shedding, those of skill in the art would be even less motivated to continue passaging the virus beyond the number of passages disclosed in D1 as some other desirable characteristic of the virus may be lost. However, that is exactly what the patentee did with the result being that 70 passages resulted in a virus that has several desirable characteristics and further eliminated shedding. This result was found to be repeatable and reproducible, and therefore, is considered by those of skill in the art to be an inherent feature of passaging. Summarizing, the subject matter of the claims as granted involves an inventive step.

In conclusion, the requests under item 1 above are well-founded.

G. Kalhammer

Dr. G. Kalhammer
Enc.:
Claims 1-16 of the 1st Auxiliary Request
Claims 1-16 of the 2nd Auxiliary Request
Claims 1-16 of the 3rd Auxiliary Request
Claims 1-16 of the 4th Auxiliary Request
Claims 1-9 of the 5th Auxiliary Request

Auxiliary Request 1

Claims

1. A vaccine composition comprising live porcine reproductive and respiratory syndrome (PRRS) virus in a modified and substantially avirulent form and mixed with a pharmacologically compatible carrier agent, said modified and substantially avirulent virus being ATCC-VR2332 virus passaged at least 70 times in cell culture of the monkey kidney cell line MA-104 such that when the modified and substantially avirulent virus is administered to a swine or other mammal prone to PRRS, it fails to cause clinical signs of PRRS disease and does not shed but is capable of inducing an immune response that immunizes the mammal against pathogenic forms of PRRS.

2. The composition as set forth in Claim 1, said modified and substantially avirulent virus being ATCC-VR2495.

3. The composition as set forth in Claim 1, said carrier agent comprising sucrose gelatin stabilizer.

4. Use of the ATCC-VR2332 virus passaged at least 70 times in cell culture of the monkey kidney cell line MA-104 to modify and render the virus substantially avirulent such that when the modified and substantially avirulent virus is administered to a swine or other mammal prone to PRRS, it fails to cause clinical signs of PRRS disease and does not shed but is capable of inducing an immune response that immunizes the mammal against pathogenic forms of PRRS for the preparation of a vaccine composition comprising a live porcine reproductive and respiratory syndrome virus mixed with a pharmacologically compatible carrier agent for the immunization of swine against porcine reproductive and respiratory syndrome (PRRS).

5. A method of producing a PRRS vaccine, comprising the steps of

   preparing a production culture of a substantially avirulent form of the ATCC-VR2332 virus, including the steps of passaging ATCC-VR2332 virus at least

70 times in cell culture of the monkey kidney cell line MA-104 to modify and render the virus substantially avirulent such that when the modified and substantially avirulent virus is administered to a swine or other mammal prone to PRRS, it fails to cause clinical signs of PRRS disease but is capable of inducing an immune response that immunizes the mammal against pathogenic forms of PRRS, and generating a production culture from the modified and substantially avirulent ATCC-VR2332 virus;
harvesting the production virus culture;
adding a stabilizing agent to the production virus culture; and
lyophilizing the production virus culture.

6. The method as set forth in Claim 5, wherein the step of preparing includes infecting the simian cell line with said virus, and incubating the resultant culture at a temperature of from about 35°C to about 37°C.

7. The method as set forth in Claim 5, wherein the step of harvesting includes freezing the virus culture.

8. The method as set forth in Claim 5, wherein the step of adding includes mixing about one part of sucrose gelatin stabilizer with about three parts of the virus culture.

9. The method as set forth in Claim 5, wherein the step of lyophilizing includes subliming moisture from a frozen sample of the virus culture.

10. The method as set forth in Claim 5, wherein said culture includes a serial volume of from 150,000 to 500,000 doses of 0.28 ml per dose.

11. The method as set forth in Claim 10 further including subdividing the serial volume prior to the step of lyophilizing.

12. The method as set forth in Claim 5, wherein said substantially avirulent virus is ATCC 2495 virus.

13. A vaccine obtainable by the method of claim 5, wherein the vaccine lacks shedding.

14. The use of claim 4, said virus being passages 75 times.

15. The composition of claim 1, said virus being passaged 75 times.

16. The method of claim 5, said virus being passaged 75 times.

Auxiliary Request 2

Claims

1. A safe vaccine composition comprising live porcine reproductive and respiratory syndrome (PRRS) virus in a modified and substantially avirulent form and mixed with a pharmacologically compatible carrier agent, said modified and substantially avirulent virus being ATCC-VR2332 virus passaged at least 70 times in cell culture of the monkey kidney cell line MA-104 such that when the modified and substantially avirulent virus is administered to a swine or other mammal prone to PRRS, it fails to cause clinical signs of PRRS disease but is capable of inducing an immune response that immunizes the mammal against pathogenic forms of PRRS.

2. The composition as set forth in Claim 1, said modified and substantially avirulent virus being ATCC-VR2495.

3. The composition as set forth in Claim 1, said carrier agent comprising sucrose gelatin stabilizer.

4. Use of the ATCC-VR2332 virus passaged at least 70 times in cell culture of the monkey kidney cell line MA-104 to modify and render the virus substantially avirulent such that when the modified and substantially avirulent virus is administered to a swine or other mammal prone to PRRS, it fails to cause clinical signs of PRRS disease but is capable of inducing an immune response that immunizes the mammal against pathogenic forms of PRRS for the preparation of a safe vaccine composition comprising a live porcine reproductive and respiratory syndrome virus mixed with a pharmacologically compatible carrier agent for the immunization of swine against porcine reproductive and respiratory syndrome (PRRS).

5. A method of producing a PRRS vaccine, comprising the steps of

   preparing a production culture of a substantially avirulent form of the ATCC-VR2332 virus, including the steps of passaging ATCC-VR2332 virus at least

70 times in cell culture of the monkey kidney cell line MA-104 to modify and render the virus substantially avirulent such that when the modified and substantially avirulent virus is administered to a swine or other mammal prone to PRRS, it fails to cause clinical signs of PRRS disease but is capable of inducing an immune response that immunizes the mammal against pathogenic forms of PRRS, and generating a production culture from the modified and substantially avirulent ATCC-VR2332 virus;
harvesting the production virus culture;
adding a stabilizing agent to the production virus culture; and
lyophilizing the production virus culture.

6. The method as set forth in Claim 5, wherein the step of preparing includes infecting the simian cell line with said virus, and incubating the resultant culture at a temperature of from about 35°C to about 37°C.

7. The method as set forth in Claim 5, wherein the step of harvesting includes freezing the virus culture.

8. The method as set forth in Claim 5, wherein the step of adding includes mixing about one part of sucrose gelatin stabilizer with about three parts of the virus culture.

9. The method as set forth in Claim 5, wherein the step of lyophilizing includes subliming moisture from a frozen sample of the virus culture.

10. The method as set forth in Claim 5, wherein said culture includes a serial volume of from 150,000 to 500,000 doses of 0.28 ml per dose.

11. The method as set forth in Claim 10 further including subdividing the serial volume prior to the step of lyophilizing.

12. The method as set forth in Claim 5, wherein said substantially avirulent virus is ATCC 2495 virus.

13. A safe vaccine obtainable by the method of Claim 5.

14. The use of claim 4, said virus being passages 75 times.

15. The composition of claim 1, said virus being passaged 75 times.

16. The method of claim 5, said virus being passaged 75 times.

Auxiliary Request 3

Claims

1. A vaccine composition comprising live porcine reproductive and respiratory syndrome (PRRS) virus in a modified and substantially avirulent form and mixed with a pharmacologically compatible carrier agent, said modified and substantially avirulent virus being ATCC-VR2332 virus passaged at least 70 times in cell culture of the monkey kidney cell line MA-104 such that when the modified and substantially avirulent virus is administered to a swine or other mammal prone to PRRS, it fails to cause clinical signs of PRRS disease but is capable of inducing an immune response that immunizes the mammal against pathogenic forms of PRRS, wherein treatment with the vaccine does not have any severe undesirable effects on the treated animals.

2. The composition as set forth in Claim 1, said modified and substantially avirulent virus being ATCC-VR2495.

3. The composition as set forth in Claim 1, said carrier agent comprising sucrose gelatin stabilizer.

4. Use of the ATCC-VR2332 virus passaged at least 70 times in cell culture of the monkey kidney cell line MA-104 to modify and render the virus substantially avirulent such that when the modified and substantially avirulent virus is administered to a swine or other mammal prone to PRRS, it fails to cause clinical signs of PRRS disease but is capable of inducing an immune response that immunizes the mammal against pathogenic forms of PRRS for the preparation of a vaccine composition comprising a live porcine reproductive and respiratory syndrome virus mixed with a pharmacologically compatible carrier agent for the immunization of swine against porcine reproductive and respiratory syndrome (PRRS), wherein treatment with the vaccine does not have any severe undesirable effects on the treated animals.

5. A method of producing a PRRS vaccine, comprising the steps of

preparing a production culture of a substantially avirulent form of the ATCC-VR2332 virus, including the steps of passaging ATCC-VR2332 virus at least 70 times in cell culture of the monkey kidney cell line MA-104 to modify and render the virus substantially avirulent such that when the modified and substantially avirulent virus is administered to a swine or other mammal prone to PRRS, it fails to cause clinical signs of PRRS disease but is capable of inducing an immune response that immunizes the mammal against pathogenic forms of PRRS, and generating a production culture from the modified and substantially avirulent ATCC-VR2332 virus;
harvesting the production virus culture;
adding a stabilizing agent to the production virus culture; and
lyophilizing the production virus culture.

6. The method as set forth in Claim 5, wherein the step of preparing includes infecting the simian cell line with said virus, and incubating the resultant culture at a temperature of from about 35°C to about 37°C.

7. The method as set forth in Claim 5, wherein the step of harvesting includes freezing the virus culture.

8. The method as set forth in Claim 5, wherein the step of adding includes mixing about one part of sucrose gelatin stabilizer with about three parts of the virus culture.

9. The method as set forth in Claim 5, wherein the step of lyophilizing includes subliming moisture from a frozen sample of the virus culture.

10. The method as set forth in Claim 5, wherein said culture includes a serial volume of from 150,000 to 500,000 doses of 0.28 ml per dose.

11. The method as set forth in Claim 10 further including subdividing the serial volume prior to the step of lyophilizing.

12. The method as set forth in Claim 5, wherein said substantially avirulent virus is ATCC 2495 virus.

13. A vaccine obtainable by the method of claim 5, wherein treatment with the vaccine does not have any severe undesirable effects on the treated animals.

14. The use of claim 4, said virus being passages 75 times.

15. The composition of claim 1, said virus being passaged 75 times.

16. The method of claim 5, said virus being passaged 75 times.

Auxiliary Request 4

Claims

1. A vaccine composition comprising live porcine reproductive and respiratory syndrome (PRRS) virus in a modified and substantially avirulent form and mixed with a pharmacologically compatible carrier agent, said modified and substantially avirulent virus being ATCC-VR2332 virus passaged at least 70 times in cell culture of the monkey kidney cell line MA-104 such that when the modified and substantially avirulent virus is administered to a swine or other mammal prone to PRRS, it fails to cause clinical signs of PRRS disease but is capable of inducing an immune response that immunizes the mammal against pathogenic forms of PRRS, wherein treatment with the vaccine has no adverse effect on body (rectal) temperature of the treated animals.

2. The composition as set forth in Claim 1, said modified and substantially avirulent virus being ATCC-VR2495.

3. The composition as set forth in Claim 1, said carrier agent comprising sucrose gelatin stabilizer.

4. Use of the ATCC-VR2332 virus passaged at least 70 times in cell culture of the monkey kidney cell line MA-104 to modify and render the virus substantially avirulent such that when the modified and substantially avirulent virus is administered to a swine or other mammal prone to PRRS, it fails to cause clinical signs of PRRS disease but is capable of inducing an immune response that immunizes the mammal against pathogenic forms of PRRS for the preparation of a vaccine composition comprising a live porcine reproductive and respiratory syndrome virus mixed with a pharmacologically compatible carrier agent for the immunization of swine against porcine reproductive and respiratory syndrome (PRRS), wherein treatment with the vaccine has no adverse effect on body (rectal) temperature of the treated animals.

5. A method of producing a PRRS vaccine, comprising the steps of

preparing a production culture of a substantially avirulent form of the ATCC-VR2332 virus, including the steps of passaging ATCC-VR2332 virus at least 70 times in cell culture of the monkey kidney cell line MA-104 to modify and render the virus substantially avirulent such that when the modified and substantially avirulent virus is administered to a swine or other mammal prone to PRRS, it fails to cause clinical signs of PRRS disease but is capable of inducing an immune response that immunizes the mammal against pathogenic forms of PRRS, and generating a production culture from the modified and substantially avirulent ATCC-VR2332 virus;

harvesting the production virus culture;

adding a stabilizing agent to the production virus culture; and

lyophilizing the production virus culture.

6. The method as set forth in Claim 5, wherein the step of preparing includes infecting the simian cell line with said virus, and incubating the resultant culture at a temperature of from about 35°C to about 37°C.

7. The method as set forth in Claim 5, wherein the step of harvesting includes freezing the virus culture.

8. The method as set forth in Claim 5, wherein the step of adding includes mixing about one part of sucrose gelatin stabilizer with about three parts of the virus culture.

9. The method as set forth in Claim 5, wherein the step of lyophilizing includes subliming moisture from a frozen sample of the virus culture.

10. The method as set forth in Claim 5, wherein said culture includes a serial volume of from 150,000 to 500,000 doses of 0.28 ml per dose.

11. The method as set forth in Claim 10 further including subdividing the serial volume prior to the step of lyophilizing.

12. The method as set forth in Claim 5, wherein said substantially avirulent virus is ATCC 2495 virus.

13. A vaccine obtainable by the method of claim 1, wherein treatment with the vaccine has no adverse effect on body (rectal) temperature of the treated animals.

14. The use of claim 4, said virus being passages 75 times.

15. The composition of claim 1, said virus being passaged 75 times.

16. The method of claim 5, said virus being passaged 75 times.

Auxiliary Request 5

Claims

1. A method of producing a PRRS vaccine, comprising the steps of

preparing a production culture of a substantially avirulent form of the ATCC-VR2332 virus, including the steps of passaging ATCC-VR2332 virus at least 70 times in cell culture of the monkey kidney cell line MA-104 to modify and render the virus substantially avirulent such that when the modified and substantially avirulent virus is administered to a swine or other mammal prone to PRRS, it fails to cause clinical signs of PRRS disease but is capable of inducing an immune response that immunizes the mammal against pathogenic forms of PRRS, and generating a production culture from the modified and substantially avirulent ATCC-VR2332 virus;
harvesting the production virus culture;
adding a stabilizing agent to the production virus culture; and
lyophilizing the production virus culture.

2. The method as set forth in Claim 1, wherein the step of preparing includes infecting the simian cell line with said virus, and incubating the resultant culture at a temperature of from about 35°C to about 37°C.

3. The method as set forth in Claim 1, wherein the step of harvesting includes freezing the virus culture.

4. The method as set forth in Claim 1, wherein the step of adding includes mixing about one part of sucrose gelatin stabilizer with about three parts of the virus culture.

5. The method as set forth in Claim 1, wherein the step of lyophilizing includes subliming moisture from a frozen sample of the virus culture.

6. The method as set forth in Claim 1, wherein said culture includes a serial volume of from 150,000 to 500,000 doses of 0.28 ml per dose.

7. The method as set forth in Claim 6 further including subdividing the serial volume prior to the step of lyophilizing.

8. The method as set forth in Claim 1, wherein said substantially avirulent virus is ATCC 2495 virus.

9. The method of claim 1, said virus being passaged 75 times.